UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/021,421	02/10/1998	RUSSEL T. JORDAN	397037	4431

30955 7590 04/13/2009

LATHROP & GAGE LLP
4845 PEARL EAST CIRCLE
SUITE 201
BOULDER, CO 80301

EXAMINER	
ANDERSON, JAMES D	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
04/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/021,421	JORDAN ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,14-21 and 34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-7, 14-21, and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 1/16/2009, are acknowledged and entered. Claims 1-3, 5-7, 14-21, and 34-36 are pending and under examination.

Response to Arguments

Applicant's arguments filed 1/16/2009 have been fully considered but they are not persuasive. Applicants argue that the Examiner's rationale for the rejection is unsound because it fails to accommodate an observed difference in kind. Applicants argue that it is impossible to separate a pharmacological composition from its functional properties, and it is absolutely necessary to consider this when assessing the patentability "of what". Applicants do not appear to have finished this sentence, but instead recite a passage from *In re Papesch*. The Examiner has carefully considered the functional properties of the claimed composition as well as the finding in *In re Papesch* but remains unconvinced that the claimed compositions are patentable over the cited prior art.

As a first matter, the fact pattern in *In re Papesch* is distinct from the fact pattern in the instant case. There, the claimed invention was chemical compounds *per se*, not compositions as here. The court, citing *In re Hass* and *In re Henze*, stated that prior case law suggests that proof of existence of unobvious or unexpected beneficial properties in a new compound, which would otherwise appear to be obvious (along with its properties), is indicative of presence of invention and hence of patentability. As with *In re Hess* and *In re Henze*, the invention of *In re Papesch* was directed to new chemical compounds rejected as being unpatentable over a single reference which discloses what is conceded to be a lower homolog of the claimed compounds. Appellants in *In re Papesch* demonstrated that the claimed compounds possessed an advantageous pharmacological property not shown to be possessed by the prior art compound. Such is not the case here. Applicants are not claiming a new compound, but rather a composition comprising 8-hydroxyquinoline, zinc bonded to said 8-hydroxyquinoline, and a carrier. As such, the facts of *In re Papesch* do not apply here.

In the context of the present claims, Applicants argue that the presumed commonality of antimycotic functionality is merely one thing to consider. Applicants assert that the allegation of obviousness is completely rebutted by a showing that the functionality differs in kind. In this regard, Applicants argue that the claimed composition is extremely potent against cancer and that they have demonstrated that a composition comprising 8-hydroxyquinoline sulfate as disclosed in the prior art is not effective against cancer or a precancer lesion. Applicants thus allege that this showing that the functionality differs in kind **from the expected antimycotic functionality** confirms patentability of the instant claims. This is an important point acknowledged by Applicants, that the claimed composition would be expected to have antimycotic activity as suggested by the cited prior art. In view of the cited prior art, one skilled in the art would be motivated to formulate a composition comprising 8-hydroxyquinoline, zinc bonded to said 8-hydroxyquinoline, and a carrier for use as an antifungal composition. The fact that Applicants have found that the claimed composition *additionally* has anticancer activity does not render the claimed compositions any less obvious.

The cited prior art teaches, suggests, and motivates one skilled in the art to formulate a composition comprising 8-hydroxyquinoline, zinc bonded to said 8-hydroxyquinoline, and a carrier. The cited prior art suggests that such a composition would be expected to have antifungal properties. Applicants have presented no evidence to rebut this expectation. As such, the Examiner is not persuaded that Applicant's determination that the claimed composition also has anticancer activity renders the claims patentable over the cited prior art. While a method of treating cancer or precancerous lesions comprising administering or applying a composition comprising 8-hydroxyquinoline, zinc bonded to said 8-hydroxyquinoline, and a carrier may in fact be non-obvious over the prior art, the claimed compositions are not.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, and 14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) (prior art of record) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) (prior art of record).

EP '207 discloses the use of water-soluble zinc-containing compounds in topical pharmaceutical compositions containing pharmacologically active agents to enhance the skin or mucous membrane penetration and retention of the pharmacologically active agent (Abstract). The preferred water-soluble zinc-containing compounds include zinc chloride as recited in the instant claims 5 and 6 (page 2, lines 42-43). Said water-soluble zinc-containing compounds are disclosed to dissociate in the topical vehicle so as to provide zinc ions for complexation or chelation with the pharmacologically active agents present in the vehicle (page 3, lines 10-12). Zinc-containing compounds are preferably present in an equimolar ratio with the pharmacologically active agents, thus meeting the limitation of instant claims 2-3 (*id.* at lines 24-25). With respect to the instantly claimed concentration of 8-hydroxyquinoline of at least 5 percent, it would have been obvious to use the same amount of active agent as the amount of the zinc-containing compound because the reference discloses equimolar ratios. Normally, use of equimolar amounts of a zinc-containing compound and pharmacologically active agent will not involve the use of escharotic amounts of zinc chloride and less than 35% zinc chloride is disclosed to be an upper limit when no escharotic effect is desired (*id.* at lines 28-31). This upper limit meets the limitation "ranging up to forty percent by weight" as recited in instant claim 5 and "less than an amount that produces an eschar in healthy mammalian tissues" as recited in instant claim 1. Other ingredients, including stability-enhancing agents and

antioxidants may be added to the disclosed compositions (*id.* at lines 35-36). With respect to the carriers recited in claim 14, the reference discloses that typical carriers include water, gel-producing materials, propylene glycol, sorbitol, etc. (page 5, lines 40-43).

With respect to the addition of the instantly claimed 8-hydroxyquinoline, EP '207 suggests that antifungal agents are suitable pharmacologically active agents for use in the disclosed compositions and discloses 8-hydroxyquinoline sulfate as a suitable antifungal agent (page 4, lines 9-31). While 8-hydroxyquinoline is not explicitly recited in the list of antifungal agents in EP '207, it is noted that Applicants disclose at page 2, lines 3-22 of their specification that 8-hydroxyquinoline is a known antifungal agent and chelating agent (see especially lines 12-14). Such is also evidenced by The Merck Index, which teaches that 8-hydroxyquinoline is a known "fungistat" used as an "antiseptic". Thus, it would have been obvious to one of ordinary skill in the art to use 8-hydroxyquinoline as an antifungal agent in the compositions disclosed in EO '207.

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to formulate a composition comprising 8-hydroxyquinoline and a chelatable metal agent such as zinc chloride. The motivation to do so is found throughout EP '207 wherein compositions comprising zinc chloride and pharmacologically active agents, including antifungal agents, are disclosed. As such, it would have been obvious to one of ordinary skill in the art that any antifungal agent, including the instantly claimed 8-hydroxyquinoline, could have been reasonably incorporated into the compositions disclosed in EP '207. Applicants' discovery that compositions comprising 8-hydroxyquinoline and zinc chloride can be used to treat epithelial lesions does not constitute a patentable distinction over the compositions disclosed in the reference. This is because a composition comprising 8-hydroxyquinoline and zinc chloride, as reasonably suggested and motivated by EP '207, is capable of performing the use recited in the instant claims.

With regard to claim 7, which recite a composition set forth in claim 1 "in combination with necrotic tissue from a lesion of said group produced by the action of said composition upon the lesion", it is noted that EP '207 teaches pharmaceutical preparations containing zinc ions and pharmacologically active agents are "injected directly into diseased tissues, particularly solid

tumors" (page 5, lines 34-38). Thus, EP '207 reasonably suggests a composition of the invention "in combination" with necrotic tissue.

Claim 15 is rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **USP No. 4,780,320** (Issued Oct. 25, 1988) (newly cited).

EP '207 and The Merck Index disclose as discussed *supra*. USP No. 4,780,320 is provided as evidence that the Pluronic series of polyoxypropylene-polyoxyethylene copolymers, marketed by BASF Wyandotte, Parsippany, N.J., contains several suitable examples if gelling polymers, such as Pluronic F127 as disclosed in Applciant's specification (Example 1). These polymers are compatible with many commonly used pharmaceutical materials, and have been approved by the FDA for medical use (col. 7, lines 31-46). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to use a gel comprising a polyoxyethylene ether derivative of propylene glycol (i.e., a Pluronic gelling polymer) as a carrier for claimed compositions. The skilled artisan would reasonably expect that such a gelling polymer would be a suitable carrier for pharmaceutical agents as taught in USP No. 4,780,320.

Claims 16-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 551 & 925-926) (prior art of record).

EP '207 and The Merck Index disclose as discussed *supra*. The Merck Index is provided as evidence that lecithin is an edible and digestible surfactant and emulsifier of natural origin used in pharmaceuticals and cosmetics (page 926). Further, dimethyl sulfoxide is disclosed as a penetrant carrier to enhance absorption (page 551). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to use lecithin and/or dimethyl sulfoxide in a carrier for pharmaceutically active agents. The skilled artisan would reasonably expect that lecithin and/or

dimethyl sulfoxide would be effective in increasing the absorption of the topical compositions disclosed in EP '207.

Claims 19-21 and 34-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **EP 0 506 207 A2** (Published 9/30/1992) in view of **The Merck Index 12th Edition** (1996, Merck & Co., publ., pages 832 (Entry 4890)) as applied to claims 1-3, 5-7, and 14 above, and further in view of **USP No. 3,637,772** (Issued Jan. 25, 1972) (newly cited).

EP '207 and The Merck Index disclose as discussed *supra*. EP '207 teaches the addition of antioxidants as additional components to the disclosed compositions (page 3, lines 35-36). EP '207 does not explicitly teach the antioxidants nordihydroguiaretic acid and ascorbic acid as recited in claims 19-21 and 34-36. However, USP No. 3,637,772 teaches that antioxidants are employed to delay the decomposition of oxidation sensitive materials and the most frequently used antioxidants include nordihydroguiaretic acid (col. 1, lines 20-35). Ascorbic acid is taught to also be used in combination with other antioxidants as a synergist (col. 1, lines 36-37 and 53). Thus, it would have been obvious to one of ordinary skill in the art to use nordihydroguiaretic acid and/or ascorbic acid as the antioxidant component suggested and motivated by EP '207. The skilled artisan would also have been imbued with at least a reasonable expectation that such antioxidants could be used as carriers for the pharmaceutical composition of EP '207.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614